REMARKS/ARGUMENTS

STATUS OF THE CLAIMS.

Claims 1, 4-9, 12, and 14-17 are currently pending in the application. Claims 1, 12, and 17 are amended herein to more clearly describe embodiments of the invention. These changes introduce no new matter and support is present in the application and claims as originally filed. The changes are made without prejudice and are not to be construed as abandonment of any previously claimed subject matter or agreement with any objection or rejection of record. Accordingly, entry of the Amendment is respectfully requested.

REJECTIONS TO THE CLAIMS

35 U.S.C. §112 Second Paragraph.

Indefiniteness

Modulate

Claims 1, 4-9 (claim 3 being previously cancelled), 12, and 14-17 are rejected in the current Office Action under 35 U.S.C. §112, second paragraph, as allegedly indefinite by failing to particularly point out and distinctly claim the subject matter regarded by applicants as the invention. Applicants respectfully traverse.

The claims were rejected as allegedly unclear in their use of the words "modulates" and "modulating." The Office Action argues that such terms are indefinite and that "neither the claim nor the specification sets forth what physical processes are intended to be encompassed in the scope of the term." The Office Action also states that the term "modulates" is "distinguished from the words 'inhibitors' and 'activators' [on the last paragraph of page 11] yet no definition is provided that sets forth what properties distinguishes a modulator from and [sic] activator or inhibitor."

Applicants submit that in addition to its plain meaning, "modulate" and its derivatives are further explained in several locations in the application as filed. For example, page 3, lines 26-30 state that

> availability of receptor, ion channels, and other molecules involved in taste transduction would permit the screening

> for **high affinity agonists, antagonists, inverse agonists, and modulators of taste cell activity. Such taste modulating compounds**... (emphasis added).

The use of "such taste modulating compounds" thus refers back to high affinity agonists, antagonists, inverse agonists, etc.

Additionally, page 5, lines 27-29, states that

> [t]he invention provides methods of **screening for modulators, *e.g.*, activators, inhibitors, stimulators, enhancers, agonists, and antagonists of TC-ICS. Such modulators** of taste transduction are useful... (emphasis added).

Such quote gives several examples of modulators (*e.g.*, activators, etc.).

Page 11, lines 29-31, states that

> **[m]odulators include** genetically modified versions of TC-ICS, *e.g.*, with altered activity, as well as naturally occurring and synthetic ligands, **antagonists, agonists**,...(emphasis added).

Thus, modulators as a group can include antagonist and agonists, etc.

Furthermore, page 26, lines 9-10, states that

> [i]n assays for identifying **modulatory compounds (*e.g.*, agonists, antagonists)**...(emphasis added).

Here too, modulators as a group include agonists and antagonists, etc.

As can be seen from such quotes, the term "modulate" and its various derivatives are used in meaning as a broader term to encompass the listed various actions that compounds can directly or indirectly have on the TC-ICS (*e.g.*, as inhibitors, activators, agonists, antagonists, etc.).

From the plain meaning of the words and from the usage in the specification, Applicants submit that the definition of "modulate" and its derivatives is not insufficient. A modulator is a compound that directly or indirectly has modulatory effect (*e.g.*, it is an activator, inhibitor, stimulator, enhancer, agonist, antagonist inverse agonist, etc.).

The use of the word "change" as a description for "modulate" in the prior Response was intended to illustrate that "modulate" can have the meaning of change in a general sense. Using "modulate" to encompass the listed actions such as "inhibit," "stimulate," act as an "agonist" or "antagonist," etc., (which are examples of changes) was thus within the scope of the word "modulate" (*i.e.*, that "modulate" encompasses such terms).

Because the term "modulate" and its derivatives are not indefinite, Applicants respectfully request that the rejection be withdrawn.

Under the influence

Claims 1, 4-9 (claim 3 being previously cancelled), 12, and 14-17 are also rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for use of the term "under the influence" in the phrase "wherein the functional effect is under the influence of the taste cell-specific ion channel subunit." Applicants respectfully traverse.

The Office Action agrees that the phrase "functional effect" has been clarified by Applicants' previous amendments, but alleges that "under the influence" is still indefinite and that it cannot be determined "what additional limitations are placed on the claim by the presence of this phrase."

Applicants believe that the phrase as used is not indefinite and that those of skill in the art would comprehend the meaning of an effect being "under the influence" of TC-ICS as describing those effects that are directly or indirectly controlled or effected by TC-ICS. Further support of such meaning can be found on page 10, lines 24-31, page 11, lines 14-22, page 23, lines 1-9, page 23, line 31 through page 24, line 32, etc., which list various effects (*e.g.*, ion concentration) that can be under the influence of TC-ICS.

TC-ICS comprises an ion channel and various effects that it can influence are listed in the cited passages, etc. Additionally, the current embodiment claimed is directed to specific functional effects under the influence of the TC-ICS (namely, changes in intracellular ion concentration, changes in transmembrane ion flux of an ion, and changes in intracellular Ca++). Applicants submit that therefore, the phrase "under the influence of" is not indefinite and would easily be understood by those of skill in the art. Because the phrase is not indefinite, Applicants respectfully request that the rejections be withdrawn.

35 U.S.C. §112 First Paragraph

Enablement

Claims 1, 4-9 (claim 3 being previously cancelled), 12, and 14-17 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse in part and amend in part.

As put forth in M.P.E.P. §2164.01, the test for enablement is whether those reasonably skilled in the art can make or use the invention based on the disclosures in the patent, along with information known in the art, without undue experimentation. In fact, it is preferable to omit that which is well known in the art. *See, e.g.*, M.P.E.P. §2164.01; *United States v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217, (Fed. Cir. 1998); and, *In re Buchner*, 929 F.2d 660, 18 USPQ2d 1331, (Fed. Cir. 1991). Just because experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. The test for undue experimentation is not just quantitative "since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *See In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The Office Action contends that in order to practice the invention, one skilled in the art "would need to know which [] assays and which materials could be used in conjunction with the polypeptide of SEQ ID NO: 8" because of the "multitude of assays, used in the art to study particular biochemical pathways involved with different aspects taste signal transduction as well as signal transduction in general."

The Office Action contends that the specification "admits that it is well recognized in the art that the signal transduction schemes underlying taste transduction are bewilderingly complex and poorly understood," and that it would require an extensive (and unduly burdensome) research plan to try to use the invention as claimed. The Office Action summarizes by stating that the "specification merely presents a laundry list of examples of the behavior of previously characterized ion channels" and that "specific details regarding the particular channel in question are need[ed] to practice the invention." Applicants respectfully traverse.

Applicants point out that the current embodiment claimed recites specific procedures (namely, tracking intracellular ion concentration, changes in transmembrane ion flux, and changes in intracellular Ca^{++}) in order to follow the functional effect, if any, of a compound on the cells/membranes comprising the sequences of the invention. Such specific recitation of uses is not an open-ended laundry list of various assays. Of course, it will be appreciated that Applicants expressly reserve the right to pursue measurement of other functional effects in further prosecution.

Notwithstanding any complexity in the various taste pathways, the assays to screen for possible changes in intracellular ion concentration, ion flux, and intracellular Ca^{++} (*i.e.*, the currently recited functional effects) in response to a putative modulator are relatively straightforward. The specification gives examples of various methods (*e.g.*, via patch clamp, etc.) to measure any changes in intracellular ion concentration, etc., that may result from a putative modulator. For example, page 25 discusses and gives examples of changes in intracellular Ca^{++} levels (and ways to measure such), changes in ion flux (and ways to measure such), etc., as well as citations to references presenting further detail and guidance.

Also, applicants point out that, as emphasized throughout the specification as filed and as evidenced by the numerous citations given within the specification, those of skill in the art are extremely familiar with, and routinely perform, assays to measure/quantify functional effects of modulators on cells/cell membranes, *e.g.*, by measuring ion flux, changes in intracellular Ca^{++}, etc. Furthermore, the level of skill in the area is quite high, and the specification cites to multiple journal articles detailing protocols to guide those of skill in the art in any experimentation.

The current claims recite three assays to test for the functional effect, if any, of putative modulators on TC-ICS. Because the level of skill in the art is high, the specification cites to numerous sources of guidance, and the types of experiments that might be needed are those that are routinely performed in the art, the breadth of the claims is fully enabled and Applicants respectfully request that the rejection be withdrawn.

The Office Action also rejects claims 1 and 17 (and presumably 12) as allegedly lacking enablement based on the requirement of forming a functional ion channel. Applicants amend.

While Applicants believe the specification is fully enabled in regard to verification of a functional ion channel, especially given the large guidance in the specification, etc., in order to further prosecution, Applicants herein amend. Thus, claims 1, 12, and 17 are amended to remove such language. Because the language upon which the rejection was based has been amended, Applicants respectfully request that the rejection be withdrawn. Applicants expressly reserve the right to pursue the prior claim language however in further prosecution.

The Office Action rejects claims 12, and 14-15 as allegedly lacking enablement because "there is no teaching of compounds that directly modulate the activity of the polypeptide of SEQ ID NO: 8." The Office Action alleges that "one of skill in the art would view the invitation to randomly sample chemicals in the hope of finding such would be unduly burdensome." Applicants respectfully traverse.

The amendment of claim 12 in the previous Response clarified the requirement of steps to identify modulating compounds. Thus, one part of claim 12 is to actually screen for/identify such compounds (which is similar to claim 1). The goal of the cited claims, *inter alia*, is to identify such compounds. Furthermore, as explained in the specification (*e.g.*, p 28, line 21 through page 30, line 30, etc.), screening of libraries for modulators and the like is very common and well known in the art. Because the identifying of modulators is one of the points/goals of the claims and it would not be unduly burdensome on a user, Applicants respectfully request that the rejection be withdrawn.

The Office Action also rejects the claims as allegedly lacking enablement for amino acids other than the sequence present in SEQ ID NO: 8 (or SEQ ID NO: 2 or SEQ ID NO: 5). Applicants amend.

While Applicants believe that the guidance of the specification is sufficient to allow determination of the recited sequence variants, alleles, etc., in order to further prosecution, Applicants herein amend claims 1, 12, and 17 to read "having an amino acid sequence selected from the group that consists of SEQ ID NO:2, SEQ ID NO:5, and SEQ ID NO:8." Again, Applicants expressly reserve the right to pursue the prior claims and other sequence variants, alleles, etc., in further prosecution and respectfully request that the rejection be withdrawn.

Written Description

Claims 1, 4-9 (claim 3 being previously cancelled), 12, and 14-17 are rejected in the Office Action as allegedly lacking adequate written description under U.S.C. §112, first paragraph. Applicants amend in part and traverse in part.

In order to satisfy the written description requirement, M.P.E.P. §2163(I) states that "a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention."

The Office Action alleges that the formation of a functional ion channel is not adequately described in the specification. Applications amend.

While, the specification describes numerous tests and assays (*see, e.g.*, pages 23-28) to use in determination of functionality of ion channels (*e.g.*, patch clamps, etc. to measure ion flux, etc.), and describes ways of defining controls to aid in determination of functionality of an ion channel (*see, e.g.*, pages 12 and 26), in order to further prosecution, Applicants herein amend claims 1, 12, and 17 to remove the limitation of "forming a functional ion channel." However, Applicants expressly reserve the right to pursue or reinstate the prior claim language in further prosecution. Because the language upon which rejection was based has been amended, Applicants respectfully request that it be withdrawn.

The Office Action alleges that claims 12, and 14-15 lack adequate written description because they do not teach compounds that modulate activity of the polypeptide of SEQ ID NO: 8. Applicants respectfully traverse.

As described above, an aspect of claims 12-15 is the identification of (*e.g.*, the screening for) compounds having a functional effect. The screening for identification of such compounds (similar to claim 1) is part of the claimed method. Applicants are not attempting to claim a broad group based on a single species as in *Fiddes*. Rather, the claims are drawn to a method of modulating taste signaling by first identifying particular compounds through their functional effect on cells/cell membranes that express the polypeptides of the invention, and then using such identified compounds to modulate taste signaling. Claims to screening/identification of compounds (and methods comprising such identified compounds) are quite common and well known in the art. Thus, because a feature of the claim is the identification of compounds that modulate SEQ ID NO:8 (or SEQ ID NO: 2 or SEQ ID NO: 5), Applicants respectfully request that the rejection be withdrawn.

The Office Action alleges that the claims are lacking in adequate written description in view of variants within 90% identity of SEQ ID NO: 8 yet which retain the required functional limitations. Applicants amend.

Again, while Applicants believe the sequence variants, etc., as claimed in the application have adequate written description support, in order to further prosecution, Applicants herein amend claims 1, 12, and 17 to be drawn to the sequence of SEQ ID NO: 8 (or SEQ ID NO: 2 or SEQ ID NO: 5) and respectfully request that the rejection be withdrawn. Again, Applicants expressly reserve the right to pursue sequence variants, alleles, etc. in further prosecution.

U.S.C. §102(e)

Claims 1, 4-6 (claim 3 being previously cancelled), 8, 12, 14, 16, and 17 were rejected under 102(e) as allegedly anticipated by US patent Publication 2002/0037515 published March 28, 2002 which claims priority to USSN 60/197,491 filed April 17, 2000. Applicants respectfully traverse.

The Office Action alleges that the Declaration of Drs. Zuker and Zhang merely presents the sequence of clone 501 and that the discussion of the Declaration in the previous Response purportedly went beyond the scope of the Declaration. Applicants submit that the Declaration does show possession of the invention prior to April 17, 2000, that the discussion in the previous Response did NOT go beyond the scope of the filed Declaration, and that all statements presented in the Response were directly supported by the Declaration as filed.

The prior Response discussed the Declaration under 37 C.F.R. §1.131 which presented the timeline of invention and showed completion of the invention prior to April 17, 2000.

As presented in the Declaration, and as detailed in the prior Response, not only was clone 501 in the possession of the Applicants prior to April 17, 2000 (Exhibit I; page 2, third paragraph; page 3, second paragraph) it had already been used as the basis of BLAST searches. (Exhibit II; page 2, fourth paragraph; page 3, second paragraph)

Such BLAST searches identified the Trpm5 mouse ortholog of the rat gene (which comprises the sequence of clone 501). (Page 3, paragraph 3). The mouse ortholog and the human Mtr1 gene were found to have a high level of homology, thus, leading the Applicants to recognize human Mtr1 as the ortholog of mouse Trpm5. (Page 3, paragraph 3). Thus, the human and mouse orthologs of the gene had been identified. Furthermore, *in situ* hybridization experiments had been

done to confirm the taste cell-specific expression of the rat version of the gene. (Page 3, paragraph 3).

Thus, the human Mtr1 gene, also known as LTRPC5 (which sequence was available prior to April 17, 2000 as an orphan ion channel) (page 2 last paragraph; Example I in specification) as well as the mouse Trpm5 gene (which sequence was available prior to April 17, 2000) (page 2, last paragraph) and the rat sequence from which clone 501 was derived by the inventors (page 2, paragraph 3) were all identified by the inventors as genes for taste cell specific ion channels prior to April 17, 2000. Once identified as taste cell-specific ion channels, the ability to screen for modulators of the channels is plain.

Thus, because the present invention was completed prior to the earliest priority date claimed by US Patent Publication 2002/0037515, such publication cannot serve as a prior art reference under 35 U.S.C. § 102(e) and Applicants respectfully request that the rejection be withdrawn.

U.S.C. §102(anticipated)

Claims 1 and 4 (claim 3 being previously cancelled) were rejected under U.S.C. §102(anticipated) as allegedly anticipated by the abstract of Bernhardt, *et al.*, *J. Physiol.*, 490:325-336, 1996. Claims 1, 2, and 4-7 were rejected under U.S.C. §102(anticipated) as allegedly anticipated by Doolin, *et al.*, *J. Gen. Physiol.*, 107:545-554, 1996. Both references allegedly anticipate the current claims in regard to SEQ ID NO:2. While the claims are currently only under examination to the extent that they read on elected SEQ ID NO:8, Applicants preliminarily address such anticipated rejections herein. Applicants respectfully traverse.

Applicants note that neither Bernhardt nor Doolin present all of the elements of the current claims. For example, neither of the cited references explicitly present the sequence of SEQ ID NO:2 as is required in the current claims. Thus, because neither of the references presents all of the elements of the current claims, neither of them can anticipate the current claims. Applicants respectfully request that the rejections be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. In the event that substantive matters are felt to remain, the Examiner is invited to telephone the undersigned at (510) 769-3507.

QUINE INTELLECTUAL PROPERTY LAW
GROUP, P.C.
P.O. BOX 458
Alameda, CA 94501
Tel: 510 337-7871
Fax: 510 337-7877

Respectfully submitted,

Paul B. Littlepage
Reg. No: 48,581